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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,589	02/12/2001	Luis Rafael Herrera Estrella	TJK/137	5829

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EXAMINER	
TAYLOR, JANELL E	
ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/701,589	ROBISON, KEITH E.
	Examiner	Art Unit
	Janell Cleveland Taylor	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 26 July 2002 .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-18 is/are pending in the application.

4a) Of the above claim(s) 8-18 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-7 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *detailed Action* .

DETAILED ACTION

1. The request filed on August 8, 2002 for a Request for Continued Examination (RCE) under 37 CFR 1.53(d) is acceptable and a RCE has been established. An action on the RCE follows. The following action is NON-FINAL.

Claim Objections

2. Claims 115 and 117 are identical in scope. Applicant is required to cancel the claim(s), or amend the claim(s) or rewrite the claim(s) so they are no longer identical.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 74, 76, 83, 84, 88, 89, 93, 95, 102, 108, 122, 124, 131, 136, and 137 are rejected under 35 U.S.C. 102(b) as being anticipated by Harms et al. (The Plant Cell, Volume 7, pages 1645-1654, October 1995).

Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA

formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645). Therefore, Harms teaches a recombinant heterologous DNA molecule comprising one or more genes that code for enzymes that synthesize organic acids, functionally linked to a promoter sequence functional in plants, and to a transcription/termination/polyadenylation sequence functional in plants. Harms also teaches that the gene is from plant origin, is associated with the chloroplast (page 1649, second column), that the promoter is a 35S promoter of CMV, that the sequence includes a transit peptide for the chloroplast or mitochondria, and that the plant is a monocot (potato plant). Therefore, Harms fully anticipates the claims.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 82, 101, and 130 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Fischhoff (USPN 5,880,275).

Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

Harms does not teach that the gene that codes for the enzyme that synthesizes organic acids is an enzyme that is located in the cytoplasm.

Fischhoff teaches "The B.t. proteins produced from the synthetic genes described here are localized to the cytoplasm of the plant cell, and this cytoplasmic localization results in plants that are insecticidally effective."

It was well known in the art at the time of the invention that transgenes may be located in the cytoplasm, as well as other organelles of the cells, such as the chloroplast, endoplasmic reticulum, or mitochondria, depending on what gene was

being expressed and where the product was intended to be. It would have been obvious that the gene would have been located in the cytoplasm, as that would have allowed for the organic acid which would have been the product, to be expressed in the cytoplasm. This would have facilitated its release into the surrounding soil, air, etc.

7. Claims 1, 3, 8-9, 22, 24, 29, 30, 62, 64, 69, 70, and 72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Sijmons (USPN 5,763,748).

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645). Therefore, Harms teaches a method for obtaining transgenic plants having an increased capacity to synthesize, to accumulate, and to exude organic acids, by integration into their genome of a recombinant heterologous DNA molecule encoding

enzymes that synthesize organic acids, involving the following steps: a) preparation of a recombinant heterologous DNA molecule encoding one or more genes for enzymes that synthesize organic acids, involving the following steps: a) preparation of a recombinant heterologous DNA molecule encoding one ore more genes for enzymes that synthesize organic acids, linked to a promoter sequence functional in plants, and to transcription/termination/polyadenylation sequence functional in plants; b) the transformation of plant cells with the recombinant DNA molecule.

Harms does not teach the regeneration of transgenic plants starting from transformed cells, or of seeds from plants obtained form these transformed cells, for one of several generations, wherein the genetic information of these transformed cells, includes the recombinant DNA molecule coding for enzymes that synthesize organic acids.

Sijmons et al. teach that a heterologous protein can be excreted by transgenic plant cells using a plant signal peptide. Sijmons teaches "After transformation of potato with the constructs...and after regeneration of adult potato plants, HSA could be detected with high specific concentration in the extracellular fluid isolated from transgenic leaf material." (Col. 7, lines 17-21). Therefore, Sijmons teaches that a transgenic potato plant may be regenerated and contain the recombinant DNA molecule.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Harms with Sijmons. This is because it would have been beneficial to regenerate the transformed plant, as it would have allowed for

the continual expression of the recombinant DNA in offspring of the transformed plants. Furthermore, it would have been obvious that to regenerate the plant because it would have allowed for further testing to be continued after the initial subject plant had died.

8. Claims 2, 5, 23, 26, 63, and 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Sijmons, and further in view of Hamilton (Proc. Nat'l Acad Sci, Vol. 93, pages 9975-9979, September 1996).

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645). Therefore, Harms teaches a method for obtaining transgenic plants having an increased capacity to synthesize, to accumulate, and to exude organic acids, by integration into their genome of a recombinant heterologous DNA molecule encoding

enzymes that synthesize organic acids, involving the following steps: a) preparation of a recombinant heterologous DNA molecule encoding one or more genes for enzymes that synthesize organic acids, involving the following steps: a) preparation of a recombinant heterologous DNA molecule encoding one ore more genes for enzymes that synthesize organic acids, linked to a promoter sequence functional in plants, and to transcription/termination/polyadenylation sequence functional in plants; b) the transformation of plant cells with the recombinant DNA molecule.

Harms does not teach the regeneration of transgenic plants starting from transformed cells, or of seeds from plants obtained form these transformed cells, for one of several generations, wherein the genetic information of these transformed cells, includes the recombinant DNA molecule coding for enzymes that synthesize organic acids.

Sijmons et al. teach that a heterologous protein can be excreted by transgenic plant cells using a plant signal peptide. Sijmons teaches "After transformation of potato with the constructs...and after regeneration of adult potato plants, HSA could be detected with high specific concentration in the extracellular fluid isolated from transgenic leaf material." (Col. 7, lines 17-21). Therefore, Sijmons teaches that a transgenic potato plant may be regenerated and contain the recombinant DNA molecule.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Harms with Sijmons. This is because it would have been beneficial to regenerate the transformed plant, as it would have allowed for

the continual expression of the recombinant DNA in offspring of the transformed plants. Furthermore, it would have been obvious that to regenerate the plant because it would have allowed for further testing to be continued after the initial subject plant had died.

Neither Harms nor Sijmons teaches that the recombinant DNA molecule comprises one or more microbial genes.

Hamilton teaches stable transfer of intact high molecular weight DNA into plant chromosomes. Specifically, Hamilton teaches transferring large amounts of foreign DNA into a plant nuclear genome, and its inherency in the progeny of the plant. Hamilton teaches that the foreign DNA may be of bacterial origin.

It would have been obvious to one of ordinary skill in the art at the time of the invention to transform a plant with a microbial gene, such as from a bacterial source. This would have been obvious to one of ordinary skill in the art at the time of the invention because it would have allowed for the foreign DNA to be expressed in the plant. This would have had many useful applications, including the harvesting of products, the ability to test the effect of the product on the plant, and for research purposes in determining gene identification and organization.

9. Claims 75, 78, 94, 97, 109, 123, 126, 114, and 115 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Hamilton (Proc. Nat'l Acad Sci, Vol. 93, pages 9975-9979, September 1996).

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid

derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

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It would have been obvious to one of ordinary skill in the art at the time of the invention to transform a plant with a microbial gene, such as from a bacterial source. This would have been obvious to one of ordinary skill in the art at the time of the invention because it would have allowed for the foreign DNA to be expressed in the plant. This would have had many useful applications, including the harvesting of

products, the ability to test the effect of the product on the plant, and for research purposes in determining gene identification and organization.

10. Claims 4, 25, and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Sijmons, and further in view of Silverman.

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

Harms does not teach the regeneration of transgenic plants starting from transformed cells, or of seeds from plants obtained form these transformed cells, for one of several generations, wherein the genetic information of these transformed cells,

includes the recombinant DNA molecule coding for enzymes that synthesize organic acids.

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It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Harms with Sijmons. This is because it would have been beneficial to regenerate the transformed plant, as it would have allowed for the continual expression of the recombinant DNA in offspring of the transformed plants. Furthermore, it would have been obvious that to regenerate the plant because it would have allowed for further testing to be continued after the initial subject plant had died.

Neither Harms nor Sijmons teach that the DNA molecule is from an animal.

Silverman et al. teaches the use of animal genes in transgenic plants. (Col. 7, lines 37-53).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use a gene encoding the enzyme that synthesizes organic acid from an animal. This is because a gene from an animal would have been readily available and would have been easily assimilated into the transgenic plant.

11. Claims 77, 96, and 125 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Silverman.

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

Harms does not teach that the DNA molecule is from an animal.

Silverman et al. teaches the use of animal genes in transgenic plants. (Col. 7, lines 37-53).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use a gene encoding the enzyme that synthesizes organic acid from an

animal. This is because a gene from an animal would have been readily available and would have been easily assimilated into the transgenic plant.

12. Claims 10, 31, 71, and 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Sijmons, and further in view of Araya (USPN 5,914,447).

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

Harms does not teach the regeneration of transgenic plants starting from transformed cells, or of seeds from plants obtained form these transformed cells, for one of several generations, wherein the genetic information of these transformed cells,

includes the recombinant DNA molecule coding for enzymes that synthesize organic acids.

Sijmons et al. teach that a heterologous protein can be excreted by transgenic plant cells using a plant signal peptide. Sijmons teaches "After transformation of potato with the constructs…and after regeneration of adult potato plants, HSA could be detected with high specific concentration in the extracellular fluid isolated from transgenic leaf material." (Col. 7, lines 17-21). Therefore, Sijmons teaches that a transgenic potato plant may be regenerated and contain the recombinant DNA molecule.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Harms with Sijmons. This is because it would have been beneficial to regenerate the transformed plant, as it would have allowed for the continual expression of the recombinant DNA in offspring of the transformed plants. Furthermore, it would have been obvious that to regenerate the plant because it would have allowed for further testing to be continued after the initial subject plant had died.

Neither Harms nor Sijmons teaches that the enzyme that synthesizes organic acids is located in the mitochondria.

Araya teaches transgenic plants including a transgene consisting of a hybrid nucleic acid sequence comprising at least one unedited mitochondrial gene fragment from higher plants.

It would have been obvious to have the enzyme located in the mitochondria. This is because it was well known in the art at the time of the invention that the mitochondria

would have allowed for the expression of the enzyme and the secretion of the organic acid of Harms. Furthermore, many genes would have been located in the mitochondria, and interactions between these genes may have been desired by one of ordinary skill in the art.

13. Claims 12, 14, 19, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Sijmons, and further in view of Ohba.

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645). Therefore, Harms teaches a method for obtaining transgenic plants having an increased capacity to synthesize, to accumulate, and to exude organic acids, by integration into their genome of a recombinant heterologous DNA molecule encoding

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It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Harms with Sijmons. This is because it would have been beneficial to regenerate the transformed plant, as it would have allowed for

the continual expression of the recombinant DNA in offspring of the transformed plants. Furthermore, it would have been obvious that to regenerate the plant because it would have allowed for further testing to be continued after the initial subject plant had died.

Neither Harms nor Sijmons teach that the transcription termination sequence is from the nopaline synthetase gene.

Ohba teaches a plant promoter and a method for gene expression using said promoter (CMV35 promoter), and a transcription termination sequence cassette originating from nopaline synthetase. (Col. 18).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the nopaline synthetase transcription termination sequence. This is because it was known in the art at the time of the invention to work well in plants, and was readily available.

14. Claims 13 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Sijmons, and further in view of Hamilton in view of Ohba.

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of

the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

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It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Harms with Sijmons. This is because it would have been beneficial to regenerate the transformed plant, as it would have allowed for the continual expression of the recombinant DNA in offspring of the transformed plants.

Furthermore, it would have been obvious that to regenerate the plant because it would have allowed for further testing to be continued after the initial subject plant had died.

Neither Harms nor Sijmons teaches that the recombinant DNA molecule comprises one or more microbial genes.

Hamilton teaches stable transfer of intact high molecular weight DNA into plant chromosomes. Specifically, Hamilton teaches transferring large amounts of foreign DNA into a plant nuclear genome, and its inherency in the progeny of the plant. Hamilton teaches that the foreign DNA may be of bacterial origin.

It would have been obvious to one of ordinary skill in the art at the time of the invention to transform a plant with a microbial gene, such as from a bacterial source. This would have been obvious to one of ordinary skill in the art at the time of the invention because it would have allowed for the foreign DNA to be expressed in the plant. This would have had many useful applications, including the harvesting of products, the ability to test the effect of the product on the plant, and for research purposes in determining gene identification and organization.

Neither Harms nor Sijmons nor Hamilton teach that the transcription termination sequence is from the nopaline synthetase gene.

Ohba teaches a plant promoter and a method for gene expression using said promoter (CMV35 promoter), and a transcription termination sequence cassette originating from nopaline synthetase. (Col. 18).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the nopaline synthetase transcription termination sequence. This is

because it was known in the art at the time of the invention to work well in plants, and was readily available.

15. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Sijmons, and further in view of Silverman and further in view of Ohba.

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

Harms does not teach the regeneration of transgenic plants starting from transformed cells, or of seeds from plants obtained form these transformed cells, for one of several generations, wherein the genetic information of these transformed cells,

includes the recombinant DNA molecule coding for enzymes that synthesize organic acids.

Sijmons et al. teach that a heterologous protein can be excreted by transgenic plant cells using a plant signal peptide. Sijmons teaches "After transformation of potato with the constructs…and after regeneration of adult potato plants, HSA could be detected with high specific concentration in the extracellular fluid isolated from transgenic leaf material." (Col. 7, lines 17-21). Therefore, Sijmons teaches that a transgenic potato plant may be regenerated and contain the recombinant DNA molecule.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Harms with Sijmons. This is because it would have been beneficial to regenerate the transformed plant, as it would have allowed for the continual expression of the recombinant DNA in offspring of the transformed plants. Furthermore, it would have been obvious that to regenerate the plant because it would have allowed for further testing to be continued after the initial subject plant had died.

Neither Harms nor Sijmons teach that the DNA molecule is from an animal.

Silverman et al. teaches the use of animal genes in transgenic plants. (Col. 7, lines 37-53).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use a gene encoding the enzyme that synthesizes organic acid from an animal. This is because a gene from an animal would have been readily available and would have been easily assimilated into the transgenic plant.

Neither Harms nor Sijmons nor Silverman teach that the transcription termination sequence is from the nopaline synthetase gene.

Ohba teaches a plant promoter and a method for gene expression using said promoter (CMV35 promoter), and a transcription termination sequence cassette originating from nopaline synthetase. (Col. 18).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the nopaline synthetase transcription termination sequence. This is because it was known in the art at the time of the invention to work well in plants, and was readily available.

16. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Sijmons, and further in view of Araya and Ohba.

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length

transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

Harms does not teach the regeneration of transgenic plants starting from transformed cells, or of seeds from plants obtained form these transformed cells, for one of several generations, wherein the genetic information of these transformed cells, includes the recombinant DNA molecule coding for enzymes that synthesize organic acids.

Sijmons et al. teach that a heterologous protein can be excreted by transgenic plant cells using a plant signal peptide. Sijmons teaches "After transformation of potato with the constructs…and after regeneration of adult potato plants, HSA could be detected with high specific concentration in the extracellular fluid isolated from transgenic leaf material." (Col. 7, lines 17-21). Therefore, Sijmons teaches that a transgenic potato plant may be regenerated and contain the recombinant DNA molecule.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Harms with Sijmons. This is because it would have been beneficial to regenerate the transformed plant, as it would have allowed for the continual expression of the recombinant DNA in offspring of the transformed plants. Furthermore, it would have been obvious that to regenerate the plant because it would have allowed for further testing to be continued after the initial subject plant had died.

Neither Harms nor Sijmons teaches that the enzyme that synthesizes organic acids is located in the mitochondria.

Araya teaches transgenic plants including a transgene consisting of a hybrid nucleic acid sequence comprising at least one unedited mitochondrial gene fragment from higher plants.

It would have been obvious to have the enzyme located in the mitochondria. This is because it was well known in the art at the time of the invention that the mitochondria would have allowed for the expression of the enzyme and the secretion of the organic acid of Harms. Furthermore, many genes would have been located in the mitochondria, and interactions between these genes may have been desired by one of ordinary skill in the art.

Neither Harms nor Sijmons nor Araya teach that the transcription termination sequence is from the nopaline synthetase gene.

Ohba teaches a plant promoter and a method for gene expression using said promoter (CMV35 promoter), and a transcription termination sequence cassette originating from nopaline synthetase. (Col. 18).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the nopaline synthetase transcription termination sequence. This is because it was known in the art at the time of the invention to work well in plants, and was readily available.

17. Claims 32, 34, 39, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Sijmons, and further in view of Croy

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

Harms does not teach the regeneration of transgenic plants starting from transformed cells, or of seeds from plants obtained form these transformed cells, for one of several generations, wherein the genetic information of these transformed cells, includes the recombinant DNA molecule coding for enzymes that synthesize organic acids.

Sijmons et al. teach that a heterologous protein can be excreted by transgenic plant cells using a plant signal peptide. Sijmons teaches "After transformation of potato with the constructs…and after regeneration of adult potato plants, HSA could be

detected with high specific concentration in the extracellular fluid isolated from transgenic leaf material." (Col. 7, lines 17-21). Therefore, Sijmons teaches that a transgenic potato plant may be regenerated and contain the recombinant DNA molecule.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Harms with Sijmons. This is because it would have been beneficial to regenerate the transformed plant, as it would have allowed for the continual expression of the recombinant DNA in offspring of the transformed plants. Furthermore, it would have been obvious that to regenerate the plant because it would have allowed for further testing to be continued after the initial subject plant had died.

Neither Harms or Sijmons teach a root-specific promoter.

Croy et al. teaches various promoters capable of use with plants, including root-specific promoters. (Abstract).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use a root-specific promoter. This is because it would have been desirable that the organic acid be exuded from the roots, and therefore it would have been obvious to use a root-specific promoter in order to produce organic acid from the roots of the plant.

18. Claims 33 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Sijmons, and further in view of Croy and Hamilton.

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid,

levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

Harms does not teach the regeneration of transgenic plants starting from transformed cells, or of seeds from plants obtained form these transformed cells, for one of several generations, wherein the genetic information of these transformed cells, includes the recombinant DNA molecule coding for enzymes that synthesize organic acids.

Sijmons et al. teach that a heterologous protein can be excreted by transgenic plant cells using a plant signal peptide. Sijmons teaches "After transformation of potato with the constructs…and after regeneration of adult potato plants, HSA could be detected with high specific concentration in the extracellular fluid isolated from transgenic leaf material." (Col. 7, lines 17-21). Therefore, Sijmons teaches that a

transgenic potato plant may be regenerated and contain the recombinant DNA molecule.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Harms with Sijmons. This is because it would have been beneficial to regenerate the transformed plant, as it would have allowed for the continual expression of the recombinant DNA in offspring of the transformed plants. Furthermore, it would have been obvious that to regenerate the plant because it would have allowed for further testing to be continued after the initial subject plant had died.

Neither Harms or Sijmons teach a root-specific promoter.

Croy et al. teaches various promoters capable of use with plants, including root-specific promoters. (Abstract).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use a root-specific promoter. This is because it would have been desirable that the organic acid be exuded from the roots, and therefore it would have been obvious to use a root-specific promoter in order to produce organic acid from the roots of the plant.

Neither Harms nor Sijmons nor Croy teaches that the recombinant DNA molecule comprises one or more microbial genes.

Hamilton teaches stable transfer of intact high molecular weight DNA into plant chromosomes. Specifically, Hamilton teaches transferring large amounts of foreign DNA into a plant nuclear genome, and its inherency in the progeny of the plant. Hamilton teaches that the foreign DNA may be of bacterial origin.

It would have been obvious to one of ordinary skill in the art at the time of the invention to transform a plant with a microbial gene, such as from a bacterial source. This would have been obvious to one of ordinary skill in the art at the time of the invention because it would have allowed for the foreign DNA to be expressed in the plant. This would have had many useful applications, including the harvesting of products, the ability to test the effect of the product on the plant, and for research purposes in determining gene identification and organization.

19. Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Sijmons, and further in view of Croy and Silverman.

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader

sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

Harms does not teach the regeneration of transgenic plants starting from transformed cells, or of seeds from plants obtained form these transformed cells, for one of several generations, wherein the genetic information of these transformed cells, includes the recombinant DNA molecule coding for enzymes that synthesize organic acids.

Sijmons et al. teach that a heterologous protein can be excreted by transgenic plant cells using a plant signal peptide. Sijmons teaches "After transformation of potato with the constructs…and after regeneration of adult potato plants, HSA could be detected with high specific concentration in the extracellular fluid isolated from transgenic leaf material." (Col. 7, lines 17-21). Therefore, Sijmons teaches that a transgenic potato plant may be regenerated and contain the recombinant DNA molecule.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Harms with Sijmons. This is because it would have been beneficial to regenerate the transformed plant, as it would have allowed for the continual expression of the recombinant DNA in offspring of the transformed plants. Furthermore, it would have been obvious that to regenerate the plant because it would have allowed for further testing to be continued after the initial subject plant had died.

Neither Harms or Sijmons teach a root-specific promoter.

Croy et al. teaches various promoters capable of use with plants, including root-specific promoters. (Abstract).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use a root-specific promoter. This is because it would have been desirable that the organic acid be exuded from the roots, and therefore it would have been obvious to use a root-specific promoter in order to produce organic acid from the roots of the plant.

Neither Harms nor Sijmons nor Croy teach that the DNA molecule is from an animal.

Silverman et al. teaches the use of animal genes in transgenic plants. (Col. 7, lines 37-53).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use a gene encoding the enzyme that synthesizes organic acid from an animal. This is because a gene from an animal would have been readily available and would have been easily assimilated into the transgenic plant.

20. Claim 41 is rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Sijmons, and further in view of Croy and Araya.

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed

by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

Harms does not teach the regeneration of transgenic plants starting from transformed cells, or of seeds from plants obtained form these transformed cells, for one of several generations, wherein the genetic information of these transformed cells, includes the recombinant DNA molecule coding for enzymes that synthesize organic acids.

Sijmons et al. teach that a heterologous protein can be excreted by transgenic plant cells using a plant signal peptide. Sijmons teaches "After transformation of potato with the constructs...and after regeneration of adult potato plants, HSA could be detected with high specific concentration in the extracellular fluid isolated from transgenic leaf material." (Col. 7, lines 17-21). Therefore, Sijmons teaches that a transgenic potato plant may be regenerated and contain the recombinant DNA molecule.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Harms with Sijmons. This is because it would have been beneficial to regenerate the transformed plant, as it would have allowed for the continual expression of the recombinant DNA in offspring of the transformed plants. Furthermore, it would have been obvious that to regenerate the plant because it would have allowed for further testing to be continued after the initial subject plant had died.

Neither Harms or Sijmons teach a root-specific promoter.

Croy et al. teaches various promoters capable of use with plants, including root-specific promoters. (Abstract).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use a root-specific promoter. This is because it would have been desirable that the organic acid be exuded from the roots, and therefore it would have been obvious to use a root-specific promoter in order to produce organic acid from the roots of the plant.

Neither Harms nor Sijmons nor Croy teaches that the enzyme that synthesizes organic acids is located in the mitochondria.

Araya teaches transgenic plants including a transgene consisting of a hybrid nucleic acid sequence comprising at least one unedited mitochondrial gene fragment from higher plants.

It would have been obvious to have the enzyme located in the mitochondria. This is because it was well known in the art at the time of the invention that the mitochondria would have allowed for the expression of the enzyme and the secretion of the organic

acid of Harms. Furthermore, many genes would have been located in the mitochondria, and interactions between these genes may have been desired by one of ordinary skill in the art.

21. Claims 42, 44, 49, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Sijmons in view of Mucchal.

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

Harms does not teach the regeneration of transgenic plants starting from transformed cells, or of seeds from plants obtained form these transformed cells, for one of several generations, wherein the genetic information of these transformed cells,

includes the recombinant DNA molecule coding for enzymes that synthesize organic acids.

Sijmons et al. teach that a heterologous protein can be excreted by transgenic plant cells using a plant signal peptide. Sijmons teaches "After transformation of potato with the constructs…and after regeneration of adult potato plants, HSA could be detected with high specific concentration in the extracellular fluid isolated from transgenic leaf material." (Col. 7, lines 17-21). Therefore, Sijmons teaches that a transgenic potato plant may be regenerated and contain the recombinant DNA molecule.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Harms with Sijmons. This is because it would have been beneficial to regenerate the transformed plant, as it would have allowed for the continual expression of the recombinant DNA in offspring of the transformed plants. Furthermore, it would have been obvious that to regenerate the plant because it would have allowed for further testing to be continued after the initial subject plant had died.

Neither Harms nor Sijmons teach that the promoter is inducible by stress caused by low phosphate availability.

Mucchal et al. teaches "an increase in phosphate uptake rate of roots and cultured and cultured cells has been observed in several plant species….Phosphate stress in yeast results in activation/inactivation of several genes associated with the pho-regulation, leading to enhanced synthesis of the high-affinity phosphate transporter and phosphatases." (page 10519, first col.)

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of Harms and Sijmons with those of Mucchal, so that the promoter is induced by stress caused by low phosphate availability. This is because phosphate is one of the major nutrients required by plants and it would have been obvious to increase the rate of phosphate uptake when the organic acid was being released in order to minimize stress on the plant.

22. Claims 43 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Sijmons in view of Mucchal in view of Hamilton.

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

Harms does not teach the regeneration of transgenic plants starting from transformed cells, or of seeds from plants obtained form these transformed cells, for one of several generations, wherein the genetic information of these transformed cells, includes the recombinant DNA molecule coding for enzymes that synthesize organic acids.

Sijmons et al. teach that a heterologous protein can be excreted by transgenic plant cells using a plant signal peptide. Sijmons teaches “After transformation of potato with the constructs…and after regeneration of adult potato plants, HSA could be detected with high specific concentration in the extracellular fluid isolated from transgenic leaf material.” (Col. 7, lines 17-21). Therefore, Sijmons teaches that a transgenic potato plant may be regenerated and contain the recombinant DNA molecule.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Harms with Sijmons. This is because it would have been beneficial to regenerate the transformed plant, as it would have allowed for the continual expression of the recombinant DNA in offspring of the transformed plants. Furthermore, it would have been obvious that to regenerate the plant because it would have allowed for further testing to be continued after the initial subject plant had died.

Neither Harms nor Sijmons teach that the promoter is inducible by stress caused by low phosphate availability.

Mucchal et al. teaches “an increase in phosphate uptake rate of roots and cultured and cultured cells has been observed in several plant species….Phosphate

stress in yeast results in activation/inactivation of several genes associated with the pho-regulation, leading to enhanced synthesis of the high-affinity phosphate transporter and phosphatases." (page 10519, first col.)

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of Harms and Sijmons with those of Mucchal, so that the promoter is induced by stress caused by low phosphate availability. This is because phosphate is one of the major nutrients required by plants and it would have been obvious to increase the rate of phosphate uptake when the organic acid was being released in order to minimize stress on the plant.

Neither Harms nor Sijmons nor Mucchal teaches that the recombinant DNA molecule comprises one or more microbial genes.

Hamilton teaches stable transfer of intact high molecular weight DNA into plant chromosomes. Specifically, Hamilton teaches transferring large amounts of foreign DNA into a plant nuclear genome, and its inherency in the progeny of the plant. Hamilton teaches that the foreign DNA may be of bacterial origin.

It would have been obvious to one of ordinary skill in the art at the time of the invention to transform a plant with a microbial gene, such as from a bacterial source. This would have been obvious to one of ordinary skill in the art at the time of the invention because it would have allowed for the foreign DNA to be expressed in the plant. This would have had many useful applications, including the harvesting of products, the ability to test the effect of the product on the plant, and for research purposes in determining gene identification and organization.

23. Claim 45 is rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Sijmons in view of Mucchal in view of Silverman.

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

Harms does not teach the regeneration of transgenic plants starting from transformed cells, or of seeds from plants obtained form these transformed cells, for one of several generations, wherein the genetic information of these transformed cells, includes the recombinant DNA molecule coding for enzymes that synthesize organic acids.

Sijmons et al. teach that a heterologous protein can be excreted by transgenic plant cells using a plant signal peptide. Sijmons teaches "After transformation of potato with the constructs…and after regeneration of adult potato plants, HSA could be detected with high specific concentration in the extracellular fluid isolated from transgenic leaf material." (Col. 7, lines 17-21). Therefore, Sijmons teaches that a transgenic potato plant may be regenerated and contain the recombinant DNA molecule.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Harms with Sijmons. This is because it would have been beneficial to regenerate the transformed plant, as it would have allowed for the continual expression of the recombinant DNA in offspring of the transformed plants. Furthermore, it would have been obvious that to regenerate the plant because it would have allowed for further testing to be continued after the initial subject plant had died.

Neither Harms nor Sijmons teach that the promoter is inducible by stress caused by low phosphate availability.

Mucchal et al. teaches "an increase in phosphate uptake rate of roots and cultured and cultured cells has been observed in several plant species….Phosphate stress in yeast results in activation/inactivation of several genes associated with the pho-regulation, leading to enhanced synthesis of the high-affinity phosphate transporter and phosphatases." (page 10519, first col.)

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of Harms and Sijmons with those of Mucchal, so that

the promoter is induced by stress caused by low phosphate availability. This is because phosphate is one of the major nutrients required by plants and it would have been obvious to increase the rate of phosphate uptake when the organic acid was being released in order to minimize stress on the plant.

Neither Harms nor Sijmons nor Mucchal teach that the DNA molecule is from an animal.

Silverman et al. teaches the use of animal genes in transgenic plants. (Col. 7, lines 37-53).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use a gene encoding the enzyme that synthesizes organic acid from an animal. This is because a gene from an animal would have been readily available and would have been easily assimilated into the transgenic plant.

24. Claim 51 is rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Sijmons in view of Mucchal in view of Araya.

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of

the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

Harms does not teach the regeneration of transgenic plants starting from transformed cells, or of seeds from plants obtained form these transformed cells, for one of several generations, wherein the genetic information of these transformed cells, includes the recombinant DNA molecule coding for enzymes that synthesize organic acids.

Sijmons et al. teach that a heterologous protein can be excreted by transgenic plant cells using a plant signal peptide. Sijmons teaches "After transformation of potato with the constructs...and after regeneration of adult potato plants, HSA could be detected with high specific concentration in the extracellular fluid isolated from transgenic leaf material." (Col. 7, lines 17-21). Therefore, Sijmons teaches that a transgenic potato plant may be regenerated and contain the recombinant DNA molecule.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Harms with Sijmons. This is because it would have been beneficial to regenerate the transformed plant, as it would have allowed for the continual expression of the recombinant DNA in offspring of the transformed plants.

Furthermore, it would have been obvious that to regenerate the plant because it would have allowed for further testing to be continued after the initial subject plant had died.

Neither Harms nor Sijmons teach that the promoter is inducible by stress caused by low phosphate availability.

Mucchal et al. teaches "an increase in phosphate uptake rate of roots and cultured and cultured cells has been observed in several plant species....Phosphate stress in yeast results in activation/inactivation of several genes associated with the pho-regulation, leading to enhanced synthesis of the high-affinity phosphate transporter and phosphatases." (page 10519, first col.)

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of Harms and Sijmons with those of Mucchal, so that the promoter is induced by stress caused by low phosphate availability. This is because phosphate is one of the major nutrients required by plants and it would have been obvious to increase the rate of phosphate uptake when the organic acid was being released in order to minimize stress on the plant.

Neither Harms nor Sijmons nor Mucchal teaches that the enzyme that synthesizes organic acids is located in the mitochondria.

Araya teaches transgenic plants including a transgene consisting of a hybrid nucleic acid sequence comprising at least one unedited mitochondrial gene fragment from higher plants.

It would have been obvious to have the enzyme located in the mitochondria. This is because it was well known in the art at the time of the invention that the mitochondria

would have allowed for the expression of the enzyme and the secretion of the organic acid of Harms. Furthermore, many genes would have been located in the mitochondria, and interactions between these genes may have been desired by one of ordinary skill in the art.

25. Claims 52, 54, 59, and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Sijmons in view of Guerinot.

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

Harms does not teach the regeneration of transgenic plants starting from transformed cells, or of seeds from plants obtained form these transformed cells, for

one of several generations, wherein the genetic information of these transformed cells, includes the recombinant DNA molecule coding for enzymes that synthesize organic acids.

Sijmons et al. teach that a heterologous protein can be excreted by transgenic plant cells using a plant signal peptide. Sijmons teaches "After transformation of potato with the constructs…and after regeneration of adult potato plants, HSA could be detected with high specific concentration in the extracellular fluid isolated from transgenic leaf material." (Col. 7, lines 17-21). Therefore, Sijmons teaches that a transgenic potato plant may be regenerated and contain the recombinant DNA molecule.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Harms with Sijmons. This is because it would have been beneficial to regenerate the transformed plant, as it would have allowed for the continual expression of the recombinant DNA in offspring of the transformed plants. Furthermore, it would have been obvious that to regenerate the plant because it would have allowed for further testing to be continued after the initial subject plant had died.

Neither Harms nor Sijmons teach that the promoter is a promoter inducible by stress caused by low iron availability.

Guerinot et al. teaches "many iron-efficient plant varieties have iron uptake strategies…that, not surprisingly, are directed at solubilizing iron….most iron deficient plants use strategy I and respond to iron deprivation by inducing the activity of membrane-bound Fe(III) chelate reductases." (Col. 1, lines 25-35).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of Harms and Sijmons with those of Guerinot, so that the promoter is induced by stress caused by low iron availability. This is because iron is one of the major nutrients required by plants and it would have been obvious to increase the rate of iron uptake when the organic acid was being released in order to minimize stress on the plant.

26. Claims 53 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Sijmons in view of Guerinot in view of Hamilton.

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

Harms does not teach the regeneration of transgenic plants starting from transformed cells, or of seeds from plants obtained form these transformed cells, for one of several generations, wherein the genetic information of these transformed cells, includes the recombinant DNA molecule coding for enzymes that synthesize organic acids.

Sijmons et al. teach that a heterologous protein can be excreted by transgenic plant cells using a plant signal peptide. Sijmons teaches "After transformation of potato with the constructs...and after regeneration of adult potato plants, HSA could be detected with high specific concentration in the extracellular fluid isolated from transgenic leaf material." (Col. 7, lines 17-21). Therefore, Sijmons teaches that a transgenic potato plant may be regenerated and contain the recombinant DNA molecule.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Harms with Sijmons. This is because it would have been beneficial to regenerate the transformed plant, as it would have allowed for the continual expression of the recombinant DNA in offspring of the transformed plants. Furthermore, it would have been obvious that to regenerate the plant because it would have allowed for further testing to be continued after the initial subject plant had died.

Neither Harms nor Sijmons teach that the promoter is a promoter inducible by stress caused by low iron availability.

Guerinot et al. teaches "many iron-efficient plant varieties have iron uptake strategies...that, not surprisingly, are directed at solubilizing iron....most iron deficient

plants use strategy I and respond to iron deprivation by inducing the activity of membrane-bound Fe(III) chelate reductases." (Col. 1, lines 25-35).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of Harms and Sijmons with those of Guerinot, so that the promoter is induced by stress caused by low iron availability. This is because iron is one of the major nutrients required by plants and it would have been obvious to increase the rate of iron uptake when the organic acid was being released in order to minimize stress on the plant.

Neither Harms nor Sijmons nor Guerinot teaches that the recombinant DNA molecule comprises one or more microbial genes.

Hamilton teaches stable transfer of intact high molecular weight DNA into plant chromosomes. Specifically, Hamilton teaches transferring large amounts of foreign DNA into a plant nuclear genome, and its inherency in the progeny of the plant. Hamilton teaches that the foreign DNA may be of bacterial origin.

It would have been obvious to one of ordinary skill in the art at the time of the invention to transform a plant with a microbial gene, such as from a bacterial source. This would have been obvious to one of ordinary skill in the art at the time of the invention because it would have allowed for the foreign DNA to be expressed in the plant. This would have had many useful applications, including the harvesting of products, the ability to test the effect of the product on the plant, and for research purposes in determining gene identification and organization.

27. Claim 55 is rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Sijmons in view of Guerinot in view of Silverman.

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

Harms does not teach the regeneration of transgenic plants starting from transformed cells, or of seeds from plants obtained form these transformed cells, for one of several generations, wherein the genetic information of these transformed cells, includes the recombinant DNA molecule coding for enzymes that synthesize organic acids.

Sijmons et al. teach that a heterologous protein can be excreted by transgenic plant cells using a plant signal peptide. Sijmons teaches "After transformation of potato with the constructs...and after regeneration of adult potato plants, HSA could be detected with high specific concentration in the extracellular fluid isolated from transgenic leaf material." (Col. 7, lines 17-21). Therefore, Sijmons teaches that a transgenic potato plant may be regenerated and contain the recombinant DNA molecule.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Harms with Sijmons. This is because it would have been beneficial to regenerate the transformed plant, as it would have allowed for the continual expression of the recombinant DNA in offspring of the transformed plants. Furthermore, it would have been obvious that to regenerate the plant because it would have allowed for further testing to be continued after the initial subject plant had died.

Neither Harms nor Sijmons teach that the promoter is a promoter inducible by stress caused by low iron availability.

Guerinot et al. teaches "many iron-efficient plant varieties have iron uptake strategies...that, not surprisingly, are directed at solubilizing iron....most iron deficient plants use strategy I and respond to iron deprivation by inducing the activity of membrane-bound Fe(III) chelate reductases." (Col. 1, lines 25-35).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of Harms and Sijmons with those of Guerinot, so that the promoter is induced by stress caused by low iron availability. This is because iron is one

of the major nutrients required by plants and it would have been obvious to increase the rate of iron uptake when the organic acid was being released in order to minimize stress on the plant.

Neither Harms nor Sijmons nor Guerinot teach that the DNA molecule is from an animal.

Silverman et al. teaches the use of animal genes in transgenic plants. (Col. 7, lines 37-53).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use a gene encoding the enzyme that synthesizes organic acid from an animal. This is because a gene from an animal would have been readily available and would have been easily assimilated into the transgenic plant.

28. Claim 61 is rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Sijmons in view of Guerinot in view of Araya.

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase

in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

Harms does not teach the regeneration of transgenic plants starting from transformed cells, or of seeds from plants obtained form these transformed cells, for one of several generations, wherein the genetic information of these transformed cells, includes the recombinant DNA molecule coding for enzymes that synthesize organic acids.

Sijmons et al. teach that a heterologous protein can be excreted by transgenic plant cells using a plant signal peptide. Sijmons teaches "After transformation of potato with the constructs...and after regeneration of adult potato plants, HSA could be detected with high specific concentration in the extracellular fluid isolated from transgenic leaf material." (Col. 7, lines 17-21). Therefore, Sijmons teaches that a transgenic potato plant may be regenerated and contain the recombinant DNA molecule.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Harms with Sijmons. This is because it would have been beneficial to regenerate the transformed plant, as it would have allowed for the continual expression of the recombinant DNA in offspring of the transformed plants.

Furthermore, it would have been obvious that to regenerate the plant because it would have allowed for further testing to be continued after the initial subject plant had died.

Neither Harms nor Sijmons teach that the promoter is a promoter inducible by stress caused by low iron availability.

Guerinot et al. teaches “many iron-efficient plant varieties have iron uptake strategies…that, not surprisingly, are directed at solubilizing iron….most iron deficient plants use strategy I and respond to iron deprivation by inducing the activity of membrane-bound Fe(III) chelate reductases.” (Col. 1, lines 25-35).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of Harms and Sijmons with those of Guerinot, so that the promoter is induced by stress caused by low iron availability. This is because iron is one of the major nutrients required by plants and it would have been obvious to increase the rate of iron uptake when the organic acid was being released in order to minimize stress on the plant.

Neither Harms nor Sijmons nor Guerinot teaches that the enzyme that synthesizes organic acids is located in the mitochondria.

Araya teaches transgenic plants including a transgene consisting of a hybrid nucleic acid sequence comprising at least one unedited mitochondrial gene fragment from higher plants.

It would have been obvious to have the enzyme located in the mitochondria. This is because it was well known in the art at the time of the invention that the mitochondria would have allowed for the expression of the enzyme and the secretion of the organic

acid of Harms. Furthermore, many genes would have been located in the mitochondria, and interactions between these genes may have been desired by one of ordinary skill in the art.

29. Claims 85 and 133 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Croy

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

Harms does not teach a root-specific promoter.

Croy et al. teaches various promoters capable of use with plants, including root-specific promoters. (Abstract).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use a root-specific promoter. This is because it would have been desirable that the organic acid be exuded from the roots, and therefore it would have been obvious to use a root-specific promoter in order to produce organic acid from the roots of the plant.

30. Claims 86 and 134 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Mucchal.

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

Harms does not teach that the promoter is inducible by stress caused by low phosphate availability.

Mucchal et al. teaches "an increase in phosphate uptake rate of roots and cultured and cultured cells has been observed in several plant species....Phosphate stress in yeast results in activation/inactivation of several genes associated with the pho-regulation, leading to enhanced synthesis of the high-affinity phosphate transporter and phosphatases." (page 10519, first col.)

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of Harms and Sijmons with those of Mucchal, so that the promoter is induced by stress caused by low phosphate availability. This is because phosphate is one of the major nutrients required by plants and it would have been obvious to increase the rate of phosphate uptake when the organic acid was being released in order to minimize stress on the plant.

31. Claims 87 and 135 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Sijmons in view of Guerinot.

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the

precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

Harms does not teach that the promoter is a promoter inducible by stress caused by low iron availability.

Guerinot et al. teaches "many iron-efficient plant varieties have iron uptake strategies...that, not surprisingly, are directed at solubilizing iron....most iron deficient plants use strategy I and respond to iron deprivation by inducing the activity of membrane-bound Fe(III) chelate reductases." (Col. 1, lines 25-35).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of Harms and Sijmons with those of Guerinot, so that the promoter is induced by stress caused by low iron availability. This is because iron is one of the major nutrients required by plants and it would have been obvious to increase the rate of iron uptake when the organic acid was being released in order to minimize stress on the plant.

32. Claims 90 and 138 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Sijmons, and further in view of Ohba.

As disclosed above, Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

Harms does not teach that the transcription termination sequence is from the nopaline synthetase gene.

Ohba teaches a plant promoter and a method for gene expression using said promoter (CMV35 promoter), and a transcription termination sequence cassette originating from nopaline synthetase. (Col. 18).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the nopaline synthetase transcription termination sequence. This is

because it was known in the art at the time of the invention to work well in plants, and was readily available.

33. Claims 110-113 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Foulkes.

Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

The claims are drawn to the transgenic plants belonging to any one of the families Poaceae, Lileaceae, Leguminoseae, Solanaceae, Caricaceae, Cucurbitaceae, Triticum, Oryza, Zea, Sorghum, Avena, Saccharum, Solanum, Lycoperisicum, or

Glycine. Harms does not teach that the transgenic plant is from one of the above-mentioned families.

Foulkes et al. teaches a large variety of plant and animal species which are transgenically altered to express the citric acid gene. (Col. 30, lines 35-60).

It would have been obvious to one of ordinary skill in the art that a variety of plant species were modifiable by a gene encoding an enzyme that encodes an organic acid. This is because many plants were known to be susceptible to increased levels of aluminum, or decreased levels of phosphate and iron, and it would have been obvious that exuding organic acid would have been beneficial to their growth and development.

34. Claims 116-117 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harms in view of Botella (USPN 6,124,525).

Harms teaches expression of a flax allene oxide synthase cDNA leads to increased endogenous jasmonic acid (JA), which is an organic acid, levels in transgenic potato plants. Harms teaches that "JA and MeJA are plant lipid derivatives synthesized from alpha-lonolenic acid by a lipoxygenase-mediated oxygenation leading to 13-hydroperoxylinolenic acid, which is subsequently transformed by the action of allene oxide synthase (AOS) and additional modification steps. AOS converts lipoxygenase-derived fatty acid hydroperoxide to allene epoxide, which is the precursor for JA formation. Overexpression of flax AOS cDNA under the regulation of the cauliflower mosaic virus 35S promoter to transgenic potato plants led to an increase in the endogenous level of JA. Transgenic plants had six-to 12- fold higher levels of JA than the nontransformed plants." (Abstract). Harms also teaches that the full length

transcript encodes a protein of 536 amino acids containing a 58-amino acid leader sequence that has the features of a mitochondrial or chloroplast transit peptide. (Page 1645).

Harms does not teach that the transgenic plants are of the Carica papaya species.

Botella teaches "The DNA sequences of the invention have utility as targets for the generation of transgenic variants of pineapple, papaya and mango in which the expression of ACC synthase is substantially inhibited to effect suppression of fruit senescence."

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of Harms with those of Botella. This is because it would have been obvious to sue the Carica papaya plant as the transgenic plant, as it was easily obtainable, inexpensive, and known for being capable of expressing transgenes.

Summary

Claims 104-107, 92, and 132 are cancelled. Claims 1-5, 8-10, 12-16, 19-26, 29-36, 39-46, 49-56, 59-66, 69-78, 82-90, 93-97, 101-102, 108-117, 130-131, and 133-138 are rejected. Claims 6-7, 11, 17-18, 27-28, 37-38 47-48, 57-58, 67-68, 79-81, 91, 98-100, 103, 118-120, 121, and 127-129 are free of the prior art and are allowable.

Conclusion

Any inquiries of a general nature relating to this application, including information on IDS forms, status requests, sequence listings, etc. should be directed to the Patent Analyst, Chantae Dessau, whose telephone number is (703) 605-1237.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janell Taylor Cleveland, whose telephone number is (703) 305-0273.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached at (703) 308-1152.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed to Group 1634 via the PTO Fax Center using (703) 872-9306 or 872-9307 (after final). The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989.)

Janell Taylor Cleveland

September 18, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600